we would like to see. So, I think there is clearly a mandate to continue to improve this product. These devices are placed in healthy individuals. So, I think it is very important to continue the effort to improve the product which is clearly fraught with problems.

So, I think I really do echo the statements that have been made both regarding informed consent and the data that is available.

DR. WHALEN: Dr. Witten, for FDA's purposes has this discussion been adequate?

DR. WITTEN: Yes, thank you.

DR. WHALEN: We, therefore, will stand adjourned for lunch and at 1:30 sharply we will reconvene.

[Whereupon, at 12:40 p.m., the panel was adjourned, to reconvene at 1:30 p.m.]

A F T E R N O O N P R O C E E D I N G S

DR. WHALEN: I would like to welcome everyone back. I would remind the public observers at this meeting that while this portion of the meeting is open to their public observation, public attendees may not participate except at the specific request of the panel.

We are now ready to continue our panel meeting with Inamed Corporations presentation.

Inamed Corporation

DR. EHMSEN: Good afternoon, Dr. Witten, Dr. Whalen, members of the panel, FDA representatives and all those in the audience. I am Ron Ehmsen, vice president of clinical and regulatory affairs for Inamed. I should point out that what had previously been McGhan Medical Corporation is now operating as Inamed Aesthetics, which is a business unit of Inamed Corporation.

My colleagues and I are here today to present an update on several conditions of approval that were associated with PMA number P990074 which covers McGhan's saline-filled breast implants. That PMA was approved by FDA on May 10, 2000 for breast augmentation in women over 18 years of age and for breast reconstruction.

There were five conditions of approval. First was a post-approval study; second, a focus group study aimed at clarifying or trying to understand whether the patients themselves had any questions about the brochures that were provided to them to help them make a choice. Third is a retrieval study. Fourth is fatigue testing and fifth is shelf-life testing.

We will break up the presentation into several parts. Dr. Audrey Weiss, our senior manager of clinical research, will present the results of the post-approval study and then we will move on from there with Kim Croyle, our senior regulatory affairs specialist, and Tom Powell, our director of technologies. Audrey?

DR. WEISS: Thanks, Ron. Inamed's first condition of approval was to conduct a post-approval study to identify long-term outcomes associated with McGhan's saline-filled breast implants.

First I would like to review the data that formed the basis of the original PMA that was submitted. The original PMA included data from three years of follow-up, three-year post-implant information from two five-year clinical studies.

Additionally, women enrolled in these studies also had begun to complete some of their three-year follow-up visits. So, limited four-year data was also available at that time.

The two clinical trials were the 1995 augmentation study which, for short, I will refer to as the A95 study. In that study, 901 patients were enrolled between 1995 and 1996 for primary augmentation. The second study was the 1995 reconstruction study, which I will refer to as the R95 study for short. That study had a very similar protocol to the A95 study and enrolled 237 patients for primary breast reconstruction. Almost all of the patients enrolled in the R95 study had had mastectomy following breast cancer, and there was a handful of patients in that study who had had prophylactic mastectomy. All of the patients in both the A95 and R95 studies had not had previous breast implants prior to enrollment.

The post-approval data collection is being conducted in two phases, and the objective of the study is to obtain long-term safety information through ten years post-implant on the same 1100 women who were enrolled in the A95 and R95 studies. Again, at the time of the original PMA complete

three-year follow-up information was available. All women had completed three-year follow-up.

So, the post-approval data collection we actually are conducting in two separate phases. The first phase has been completed, and involved continuing to follow those 1100 women enrolled in the A95 and R95 studies under the same protocols as those studies had been conducted under through three years post-implant. Specifically, the protocol involved women coming in to see their physician for a follow-up visit in the office. The four-year and five-year follow-up information that forms the phase one of the post-approval data collection was based on this method of data collection. Complete five-year information is now available. All patients have completed the five-year follow-up visit and the five-year data is what I will present today.

The second phase of post-approval data collection is currently in process. This phase involves continuing to follow those same 1100 women who were enrolled in the A95 and R95 studies using a mail survey protocol that will follow them from six to ten years post-implant. On the anniversary of their original implant surgery, patients will be

sent a mail survey to complete regarding the status of critical safety outcome variables, including reoperation and implant leakage/deflation. Again, that phase two is in process and we are currently mailing surveys to patients fort he six- to ten-year follow-up information.

The remainder of the presentation will focus on the five-year follow-up information from phase one. First, I would like to present the follow-up compliance information for patients enrolled in the A95 and R95 studies.

First, what I have done here is actually included the follow-up compliance rate at each of the required follow-up intervals, which was annually through the five years in the A95 and R95 clinical studies. The data that was presented for the original PMA was three-year data which was based on 83 percent patient compliance for the augmentation cohort and 88 percent follow-up compliance for the reconstruction group.

For the post-approval phase the follow-up compliance rate has remained at 80 percent or higher. At five years the follow-up compliance rate was 81 percent for augmentation patients and 80 for the reconstruction patients.

Next, I would like to present the information obtained for specific local complications that were assessed in the A95 and R95 studies. The specific complications that I will present are reoperations, implant replacement/ removal, leakage/deflation, capsular contracture, infection, and a variety of other complications that were included in the protocols and, for completeness, we have included them here today. These include complications such as surgical-related outcomes including hematoma, seroma, and skin and nipple related complications.

I should point out with this complications that these are not additive. The same patients who are included in the reoperation rate, for example, may also be included in implant replacement/removal since implant replacement/ removal is a subset of reoperations. Similarly, a patient may undergo a leakage/deflation and also be included in the risk for implant replacement/removal. So, they are independent risks and are not additive.

Again, the method used for data collection was a physical examination by a physician at an office visit, according to the original protocol for the A95 and R95 studies. The analysis method

utilized was a cumulative risk based on the Kaplan-Meier product limit method with 95 percent confidence intervals computed. The cumulative risk that you will see in the following graphs is represented as a failure rate curve which, you will see, increases or stays level over time. It will never go down because, as we add additional events in over time the risk can only increase.

What you will see in the cumulative risk curves is the summation of all events that occurred up to the particular time point being reported, and each of the time points that were assessed in the study is presented.

What I will do now is go through each of the specific complications, reoperations, implant replacement/ removal, leakage/deflation, capsular contracture and infection and report on the risk information obtained through five years post-implant.

First, this graph represents the cumulative risk of reoperations for the augmentation and reconstruction patients. Again, the risk is being presented for each of the time points that were assessed in the study, and you can look at this as a cumulative risk through the time

point presented in the graph. The white line represents the cumulative risk for the augmentation patients and the yellow line represents the cumulative risk for the reconstruction patients.

For example, with reoperations the cumulative five-year risk for augmentation patients is approximately 25 percent and the cumulative risk of experiencing at least one reoperation through the five-year time point is approximately 42, 43 percent.

Next, what I would like to do is breakdown what types of reoperation procedures patients underwent. The reoperations reported here include any type of operative procedure to the breast or chest area, for example, implant replacement/removal and biopsy/lump removal, for example, is included here.

The next graph will break down for all those patients who underwent reoperation what those reoperations were. This pie chart represents the breakdown of all of the reoperations for augmentation patients. What you can see here from the red wedge is that the largest proportion, the largest number of reoperations were implant replacement/ removal. That could be removal with

or without replacement of the device.

The second most common type of reoperation performed for the augmentation patients was a capsule procedure, for example, capsulotomy or capsulectomy.

For reconstruction patients, the breakdown of the types of reoperation procedures is as such. Again, implant replacement/removal is the most common type of reoperation performed, followed by, in the purple wedge, scar revision or wound repair, and then capsule procedures.

What I will do next is drill down into this chart a bit and look specifically at the most common type of reoperation, which is implant replacement/removal, and look specifically at risk through five years of that particular reoperation and then look at reasons why patients undergo implant replacement/removal.

First, this graph represents the cumulative risk through each of the time points indicated, ending with the five-year time point, of implant replacement/removal for augmentation and reconstruction patients. Through five years, the risk of experiencing an implant replacement/ removal was approximately 11 percent for

augmentation patients and approximately 28 percent for reconstruction patients.

The next two graphs will look at these patients who have undergone implant replacement/removal and look specifically at why patients underwent the device replacement/removal.

First for augmentation patients, the most common reason why patients undergo replacement/removal is seen with the red wedge, which is the patient's own choice to change the size or the style of the device. The second most common reason for device replacement/removal is leakage/deflation of the device.

For reconstruction patients the predominant reason for undergoing implant replacement/removal is capsular contracture, followed by the patient's choice to change the size or style of the device, and then leakage/deflation.

The next slides that I will present break out these particular complications that have been represented in these graphs and look specifically at the risk to patients of experiencing various complications, including leakage/ deflation, capsular contracture and infection.

This graph represents the cumulative risk

through five years for augmentation patients and reconstruction patients who experienced a leakage/deflation. As you can see, the risk is virtually identical for both augmentation and reconstruction patients, and is approximately six percent through the five-year time point.

For capsular contracture, the five-year cumulative risk for augmentation patients is approximately ten percent and approximately 35 percent risk through five years for reconstruction patients.

Next is the risk of infection following implant surgery. For augmentation patients through five years the risk of experiencing an infection is approximately one percent and for reconstruction patients approximately five to six percent.

The remaining graphs that I will show for the local complications that were assessed in the A95 and R95 studies are actually summaries of the cumulative Kaplan-Meier risk curves that you see here. We had another approximately 20 or so complications that were assessed in the A95 and R95 studies, and for completeness I have included them here. Each one of them, you can imagine, has a Kaplan-Meier risk curve, just like those

complications presented here. However, for brevity, what I have done is include them on a bar chart that summarizes only the five-year risk rate, which would be the highest possible risk through five years.

For example, this graph includes six implant-specific complications, and what you see with the white bar is the risk through five years for augmentation patients, and the yellow bar, the risk through five years for reconstruction patients.

For example, the risk of experiencing asymmetry for an augmentation patient through five years is approximately 12 percent, and for reconstruction patients approximately 40 percent.

In discussions with clinicians, they have indicated that this is to be expected given that with reconstruction patients they are trying to match a reconstructed breast that has had mastectomy with a normal non-reconstructed breast on the other side.

Also reported here are cumulative five-year risks for capsule classification, implant extrusion, implant malposition, implant palpability and wrinkling.

The next graph reports the five-year cumulative risk for augmentation and reconstruction patients for various surgical-related complications that were assessed in these studies. As you can see from this graph, all of these surgical-related risks occurred at well less than ten percent, actually under seven percent for the five-year cumulative risk. Presented are delayed wound healing, hematoma, scarring, irritation/inflammation, lymphadenopathy, pneumothorax and seroma.

The next graph presents the cumulative five-year risks for various skin and nipple-related complications that were assessed in the A95 and R95 studies. Presented are the risks for loss of nipple sensation, nipple paresthesia, skin paresthesia, skin rash, tissue/skin necrosis and breast pain.

The next graph that I will present looks very similar to this, however it differs in two very important ways. Following implant replacement, we continued to follow patients and look at any outcomes following the replacement, and this graph looks at the cumulative risk of some specific complications following device

replacement.

The two critical differences in this graph that I would like to point out from the ones that you have seen previously are, first, that the risk presented here is at three hears following replacement. Patients were able to be revised any time through the five years. So, limited follow-up information is available for patients, for example, who were explanted at year four. We would only have one year of information following the device replacement. So, we were only able to calculate a valid risk with the information available for three years following the replacement in the study.

The second difference in this graph is that, unlike the previous risk information presented which was on a by-patient basis, this analysis is based on a by-device or by-implant basis. This was selected because patients could have one side revised rather than both sides. So, it made the most sense to look specifically at an analysis by the replaced device.

The complications presented here are of second replacement removal following replacement removal. The risk here, you can see, is approximately 18 percent three years following

replacement for augmentation patients and approximately 28 percent for reconstruction patients; risk of leakage/deflation following device replacement; risk of capsular contracture and risk of infection following a replacement surgery.

Next, I would like to present information obtained on reports of breast cancer post-implant and connective tissue or autoimmune disease reports. First for breast cancer, of the 901 enrolled augmentation patients, there was one post-implant report of breast cancer which occurred 27 months after implant surgery. For reconstruction patients, there were 24 post-implant reports of breast cancer through five years post-implant. All of these 24 reports occurred in patients who previously had had breast cancer, which was the reason why they enrolled in the study initially. The cancer may have recurred in the same breast that originally had the breast cancer or in the contralateral side.

Next, connective tissue and autoimmune disease information, the method of data collection for connective tissue and autoimmune diseases was that a patient would self-report to her physician

that she had a particular connective tissue or autoimmune disease. Based on the self-report by the patient, the physician would attempt to contact a diagnosing physician, attempt to obtain a diagnosis by the rheumatologist for example. If the physician was able to obtain a diagnosing physician's report we term that here a confirmed report. In other words, there is a physician diagnosing the patient with the particular connective tissue or autoimmune disease. If the patient self-report was not able to be confirmed by a diagnosing physician's report, we list that here as an unconfirmed report. It is still a patient's self-report of the disease but the doctor has been unable to obtain a diagnosing physician's report. That may be due either to the patient never obtained the diagnosis or is not able to be contacted, for example.

Additionally, and I do not report that here, there have been some cases of self-reports by patients that have been found to be false reports, where the patients initially reported a particular connective tissue or autoimmune disease and subsequently indicated that they actually either had a different type of diagnosis or did not have a

connective tissue or autoimmune disease at all.

For the augmentation group, there were 7 confirmed reports of connective tissue or autoimmune disease and 13 unconfirmed reports. Of the 7 confirmed reports, 3 were Grave's disease, 2 were hyperthyroiditis and 2 were chronic fatigue syndrome or fibromyalgia.

Among the reconstruction patients there was one confirmed report of a connective tissue or autoimmune disease and four unconfirmed reports. The one confirmed report was a diagnosis of Grave's disease.

Last, I would like to present information obtained concerning patient satisfaction with their breast implants. At each follow-up interval with their physician, patients were asked whether they were satisfied or dissatisfied with their breast implants and breast implant surgery. The following graph presents the results from each annual follow-up visit so it includes data from the original PMA through three years, as well as the post-approval data at four and five years. It indicates the percentage of patients who indicated that they were satisfied with their breast implants.

For the augmentation cohort, you can see that the percentage has been at 95 or 96 percent of patients at each annual follow-up visit, including five years post-implant, with 95 percent of augmentation patients indicating they were satisfied.

For reconstruction patients the percent of patients indicating they were satisfied has remained at around approximately 90 percent, with 88 percent indicating they were satisfied at three years post-implant and 89 percent indicating they were satisfied at five years post-implant.

To conclude the information pertaining to the post-approval study, Inamed is conducting its post-approval study in two phases. The first phase has been completed and involved continuing to follow patients enrolled in the A95 and R95 studies out through five years post-implant, according to those original study protocols which involved physician examination of the patient at an office visit.

The second phase is ongoing, and Inamed is in the process of obtaining mail surveys from patients who will self-report on the status of their breast implants out through ten years

post-implant.

Next, I would like to turn the presentation over to Kim Croyle, senior regulatory affairs specialist with Inamed, who will talk about the second condition of approval, which is the focus group study.

MS. CROYLE: Thank you, Audrey. Good afternoon, panel.

In order to meet the second PMA condition of approval, Inamed contracted with Kaplan West Qualitative Research Organization to conduct a focus group study in order to obtain women's opinions and assessment of our patient brochure.

The research objectives of the focus group study were to obtain women's feedback regarding the quality of our patient brochure, and to propose qualitative changes to improve the patient brochure, based on the study findings.

There were six focus groups consisting of 8-13 women each, three groups for augmentation, which consisted of two groups of women who had had, or who were considering, or had considered breast augmentation; one group of women who had previously had breast augmentation. Additionally, we had three reconstruction groups, two groups of women

who had considered or were considering breast reconstruction, and a third group of women who had previously had breast reconstruction.

The key findings in discussion with the patients who were participating and the women who were considering these surgeries were that the brochure was informative, and also was helpful to them and answered most of the patients' questions. So, we had a lot of positive feedback, particularly regarding the fact that the brochure did provide them with potential risks and complications, the surgical procedures. It proposed questions they could ask their surgeon about their surgery. The impact the implants might have on mammography, and their other interest was knowing about the style and size options available.

An additional finding of the assessment from all these women was that the brochure was so comprehensive and extensive that it created some confusion. There was a lot of information for them to have to, you know, review and assess. Their key comments were difficulty in understanding and interpreting the clinical tables. Most of the women found it king of daunting to understand the tables. Finding, within the brochure, relevant

sections was important to them. Also, difficulty in understanding how the brochure was actually organized, where they would find the information they needed and the graphic presentation.

As a result of their comments and feedback, we have incorporated changes to the patient labeling and provided that to FDA. Part of the changes that we have implemented are revisions to the clinical tables to make them easier to understand and clearer. We have created separate sections for augmentation and reconstruction because the women who provided feedback on this point wanted to find the surgery that pertained to them, whether it be augmentation or reconstruction. We also added a table of contents and a glossary of terms, and we modified the graphic presentation for ease of use. This condition of approval the FDA has determined we have completed.

Now I will pass the microphone to Tom Powell.

MR. POWELL: Good afternoon. The third condition of approval involved an effort to determine mode of failure of saline implants. The objective of this retrieval study was to use reported and observed information to understand and

identify possible mode of implant failure.

In the eight months from July of 2000 to March of 2001, over 2000 saline devices were returned as deflated and were evaluated. This quantity represents in the neighborhood of a half percent of the devices that were sold.

Evaluations included detailed visual examinations, the interpreting physicians' reports and performing appropriate testing, such as shell, material, mechanical tests.

From this effort, failure characteristics were identified and grouped into the following categories: smooth-edge opening, shell openings associated with a crease or fold, which is indicative of a true device failure as this characteristic is nearly always associated with deflation.

Sharp-edge opening, openings in the device shells where there is no associated crease. The reason for this characteristic is yet undetermined and may be a true failure or an artifact from handling, and are associated with both reported deflated and non-deflated retrieved implants.

Valve delamination, a characteristic where 50 percent or more of the valve bond area is lost.

For devices where valve observations confirmed physician reports, this may be representative of a true device failure. However, based on lab identification of valve delaminations on non-deflated retrieved implants, this characteristic may be the result of an artifact.

Leaky valve, this characteristic is identified by a device demonstrating leakage upon return evaluation. The reason for this characteristic is unknown and may be most likely a result of an artifact as it is frequently associated with non-deflated retrieved implants found in the lab to have a leaky valve.

Additionally, another group of devices was identified as returned devices reported as deflated where lab evaluation could not confirm the deflation characteristic. These devices were determined by lab evaluation to be functional and the devices in this group made up approximately 10-15 percent of returned reported deflated implants.

The next condition of approval was continued activity on fatigue testing, responding to past concerns. These were testing of minimum thickness products; controlling the compression by

load values rather than the displacement technique previously employed; and testing of the individual units rather than simultaneously testing multiple units.

Specific equipment was purchased to address these concerns and a protocol was accepted. The smallest size was selected as worst case where the load is concentrated over the smallest area. The test duration was accepted at either device failure or at 6.5 million cycles. The acceptance criteria was accepted to be all samples passing the anticipated in vivo load of 5 lbs, all samples pass ingredients twice the anticipated in vivo load, and evidence that the anticipated in vivo load is past the inflection point, or elbow point, defined as the intersection of the best-fit log curve with the linear best-fit curve from test values.

Results demonstrated that all criteria were met. All samples passed at both 5 lbs and 10 lbs, and the endurance limit or the threshold force below which an implant can undergo the run-out number of cycles without failure was determined to be 20 lbs. The ultimate static force value was used in determining the inflection point and the in vivo load anticipated at 5 lbs was clearly

underneath the inflection point of 44 lbs for smooth products and 48.5 lbs for textured implants.

The last condition of approval was to initiate a real-time study to support a five-year shelf life. Currently, saline implants have approval for a four-year shelf life at Inamed.

To support this five-year dating, all test product was subjected to shipping simulation and testing of both packaging and product is ongoing. For packaging performance, four test criteria is evaluated, and those are those up on the screen. The results for the year zero are also up there. For product performance seven categories are tested and, again, the results for year zero have all passed and testing is ongoing.

I will turn the microphone back to Ron.

MR. EHMSEN: Thank you, Tom and Kim and Audrey also. Just to quickly summarize, the five-year follow-up, as part of the post-approval study, has been completed and the years six through ten are in process at this point.

The focus group study has been completed. The final report for the retrieval study is being prepared and will be submitted to FDA very shortly.

The fatigue testing has been completed,

and the baseline or year zero values for shelf life testing have also been completed, and this will continue on for a period of five years.

I would like to open the floor to questions at this time. We are joined to today by Dr. Scott Spear, who is professor and chief of the Division of Plastic Surgery at Georgetown University, who may be able to address clinical questions if you have any; also, Joanne Kune, our director f regulatory affairs at Inamed. We also have several key members of our technical staff, Meggy Backstrand who is our senior biostatistician and contributed greatly to the preparation and organization of this data, Farhan Jahab, who is our group leader for device analysis, and Mike Taylor, our process validation group leader. So, if you have any questions, we would be happy to try to answer them.

DR. WHALEN: Thank you. If I could begin, perhaps Dr. Weiss, you described in one of your slides that was labeled implant-specific complications"and I have a couple of questions. One was labeled implant malposition and just looking at those two words, I would have thought that would have been on the next slide in terms of

a surgeon complication rather than the device. Could you elaborate on what implant malposition is? In other words, if somebody comes out with breast augmentation at their right knee, that seems to me to be the surgeon and not your device. How do you explain that?

DR. WEISS: I am actually going to defer this to Dr. Spear to answer.

DR. SPEAR: My recollection is that we wanted to be as encompassing as we could in terms of things that could be related to the implant so, for example, an implant could be put in the right position but, because of its properties or characteristics, it might displace itself. So, although it could be surgeon related in terms of making a space where it shouldn't be made, it could also be device related. So, I think it is just meant to be as generous as possible.

DR. WHALEN: So, if it was in the right place when I finished is sort of like it was dry when I closed?

DR. SPEAR: It could be.

DR. WHALEN: The same sort of thing? Thanks. On that same slide, Dr. Weiss, what is implant palpability?

DR. WEISS: Implant palpability would be that you could actually feel the device through the skin.

DR. WHALEN: So, the ones that you have on your slide are ones where you can--

DR. WEISS: The surgeon noted it as a complication, that they could actually feel the device through the skin.

DR. WHALEN: So, it is moderately subjective.

DR. WEISS: It would be based on physician assessment.

DR. WHALEN: Correct. Finally, Dr. Weiss, my last question for you, in the patient satisfaction data that you reported, those are percentages of patients with implants remaining in place?

DR. WEISS: Correct.

DR. WHALEN: Other questions? Dr. DeMets?

DR. DEMETS: As a follow-up of some of the follow-up studies, do I understand that no patients were excluded from your analysis? I didn't hear you comment on that. The patients that you started out with, they are all in the Kaplan-Meier curves for example? There were no patients excluded?

DR. WEISS: That is correct, no patients were excluded.

DR. DEMETS: And how did you handle the situation for the issue of censoring that we discussed earlier today for patients who had the implant removed?

DR. WEISS: There was no specific correction that was taken into account in the Kaplan-Meier analysis. The follow-up compliance rate was at 80 percent or above. So, we did not do any type of bias analysis at this point.

DR. DEMETS: So, any complication that took place in a patient in whom the implant was removed, at least it counts up until that point in time in all the graphs? For some outcomes it is not relevant; for some it might be.

DR. WEISS: Correct, if the patient was lost to follow-up or was explanted of all study devices at a particular point, her data up to the time that she either dropped out of the study or had all of her devices explanted was included. If she was replaced with another study device, the outcomes associated with the replacement continued to be followed and those were reported here.

DR. DEMETS: While I think that your

response rate is certainly pretty good, 80 percent, for reasons I said earlier it may not be good enough because of the kind of attention that this device is drawing. But do you have any sense of the potential bias that might be in the non-responders? You can't do a very thorough job of this, but have you looked at this at all?

DR. WEISS: I don't have anything specifically for this study. I know that in some of our other studies we have found that some of the reasons why patients have not returned for follow-up visits have included being unable to because they are out of the country, for example, or have been in an accident. So, we have had some information to suggest some reasons why patients don't return.

DR. DEMETS: If I understood you correctly, the information up to the five years was obtained through patient visits to their surgeon and/or the clinical site?

DR. WEISS: That is correct. It was a visit to their same physician with whom they had enrolled in the A95 or R95 studies. Or, potentially a follow-up physician if the patient moved to another area, for example, she could see

another physician in her area.

DR. DEMETS: And, do I understand that you are proposing for the five- to ten-year to do more of a questionnaire?

DR. WEISS: Correct. The six- to ten-year follow-up is being obtained via a mail survey to those patients.

DR. DEMETS: Thank you.

DR. WHALEN: Questions for Ms. Croyle, you reported your focus groups were confused about the clinical tables. Have you taken some actions to redesign that data presentation? Confusion is sort of a non-descript word. Can you elaborate a little further on that?

MS. CROYLE: Confusion may not be the most accurate term. A lot of women are not familiar with looking at that type of information. It is just something they typically won't look at unless they are in academia or they have a job where they are utilizing tables. I think it was more just an understanding, comprehension issue.

DR. WHALEN: In that regard, I know each PMA stands on its own and, therefore, every update stands on its own so I don't want to be comparing one to the other, but there was the opinion voiced

earlier that when people looked at some of the data for the other sponsor, they just couldn't believe it was that high and they just thought they were covering their own derrieres in that regard.

MS. CROYLE: We did not have any of that kind of feedback. That was information we did not receive.

DR. WHALEN: So, phrased another way, was it the perception of your independent contractor doing your focus groups that women looking at your complication rates grasped what that meant?

MS. CROYLE: They grasped what we were trying to do; it was just daunting. Based on the review, they were allowed to read the brochure prior to the interviews, and most of the feedback from many women, not all--I actually sat in and viewed most of these focus groups in the two-way mirror, and most of them just said I don't really need this. It is not very helpful to me. It is not the sort of thing I would utilize. Other women would say I would need to study it further; I am not sure what these tables are telling me.

DR. WHALEN: Dr. Choti?

DR. CHOTI: Ms. Croyle, regarding the focus group, you had some comparison groups. You

had some augmentation focus groups prior to and then a group of women after, as well as the reconstruction. I am curious whether you saw any differences between the different focus groups.

MS. CROYLE: I would say the main observation of those who had reconstruction or augmentation was that they very much appreciated that this information was available. Many of them had had surgery quite a few years previously and they felt that if they had all this additional information at that time it would have been helpful. So, it was mostly positive feedback from those who had had the experience. There were a few who said, you know, if I had had this knowledge I might have made a different decision, but it was primarily that it was more informative and helpful.

DR. CHOTI: Another question to Dr. Weiss, it is interesting that when looking at the local complications I would have expected, if anything, the number to go up, that is, the shape of the curve to be different than an asymptotic curve. At least the reoperation curve was kind of asymptotic, higher number in the first year than the second and so forth, which perhaps may be related to exchange of implants, and so forth. But even with deflation

one might expect that to go up over time, greater in the fourth year, the third, the fourth and the fifth year than in the first year. If I recall, your curve was quite linear. Any speculation as to why we are seeing that?

DR. WEISS: Not really. I don't have any suggestions as to why that may be occurring. I will defer to Dr. Spear again.

DR. SPEAR: I don't claim to be a biomaterials expert, but I think we heard about this issue of the inflection point with these devices, and I think the expectation is that they will wear at a fairly linear rate up to some point, at which point the failure rate we expect will accelerate. It is just that at five years it doesn't accelerate. It might be at ten years or 15 years, or 25 or 30 years. I don't know if Tom has any comment about that.

MR. POWELL: I think it would be hard to assess a time expectancy of this implant because of the flexibility and the forces of the body counteract that to some extent and fix it in place. So, it is a very challenging area for investigation, but I would not really have a good response to that question at this time.

DR. CHOTI: I do want to compliment you on what I thought was very clearly presented.

DR. WHALEN: Dr. Dubler?

DR. DUBLER: I have two questions. First on the focus groups, when you went back to them, you had your focus groups redesign your brochure and then brought it back. Is that correct?

MS. CROYLE: No, the focus group studies were conducted to revise the approved labeling for the PMA.

DR. DUBLER: All right. And, you said that people found the tables confusing, or whatever word we are now using.

MS. CROYLE: Right. Difficult.

DR. DUBLER: Difficult, fine. Have you removed the tables and substituted--

MS. CROYLE: No, the tables are still there because they certainly contain key information, but the language, the explanatories introducing the tables have been expanded and we have worked with the FDA quite some time on trying to make that much more comprehensive for the patients.

DR. DUBLER: So, even if you don't read the table, you will get the information?

MS. CROYLE: You will certainly get a brief gist of the contents of the table, yes.

DR. DUBLER: My second question, and I am not sure to whom to address it, is that the data for your R95 have substantially greater complication rates than for your A95. Speculation why? Is the reconstruction happening too soon? It is so startling in all of the data that I wonder if you have begun to think that perhaps ways of changing surgeon practice might reduce those high rates. I am a little puzzled about why they are so high.

DR. WEISS: I will ask Dr. Spear to address this.

DR. WHALEN: If he can figure out how to change surgeon practice, he will get the Nobel Prize.

DR. SPEAR: I wish we could. Actually, it is not surprising from the clinical point of view. It is pretty much expected. In fact, if you want to get technical, since these are per-patient complications and many reconstructions are unilateral, the data is probably even more disparate because the per-device complication is probably even higher in reconstruction than it is

in augmentation because there are two in augmentation and in reconstruction there is only one device.

But, you know, they are two operations. There is underlying scar tissue. There is often radiation involved. It is a much more technically challenging situation, and it is a fluid situation. Frankly, the standards of practice in 2002 are different than they were in 1999 or 2000 because of changing patterns of treatment of breast cancer. So, it is to be expected that the complication rate would be higher.

What is very interesting from an academic point view is that the one complication rate which is the same is the failure rate, which is not specific to the underlying environment that is device specific. The failure rates are actually identical.

DR. WHALEN: Dr. Newburger?

DR. NEWBURGER: Have you noticed any difference in the failure rates of the implants related to the positioning of the implants? In other words, is there less of a leakage rate if it is inframuscular as opposed to supramuscular? Is there any complication rate that you can relate to

positioning? For example, the skin and nipple complication rates are reasonable. Are these related to periareolar positioning?

DR. WEISS: That was not a focus of the study, to look at differences, although there was a secondary analysis that had been conducted at the time of the original PMA that looked at submuscular versus subglandular placement on certain select variables, including leakage/deflation and at the time that data, I believe, three-year rates were available and there was no difference observed at that time.

DR. WHALEN: Ms. Brown?

MS. BROWN: First I would like to compliment the company on getting 80 percent follow-up out to five years. Getting patients back to the doctor's office I think is probably a pretty big challenge so I compliment you on that.

I was intrigued by the satisfaction rate of 90-95 percent in the context of reconstructive contracture rates of 35 percent, if I understood that correctly, and augmentation contracture rates of 10 percent, and leakage/deflation rates a little less than 10 percent in both those populations. I just find that really interesting, that patients

were that satisfied when they are having those kinds of rates of contracture and leakage. I was curious as to the 5-10 percent who weren't satisfied, if you have some thoughts on why they weren't satisfied, either the contracture patients, the leakage patients.

DR. WEISS: I don't specifically have that information with me. We did have the physician ask if the patient was not satisfied, why she wasn't and she would provide a reason, and I don't have a synopsis of that information, but they could list a complication, for example, as a reason.

MS. BROWN: I also thought it was a good indication that perhaps the informed consent process is working if 90-95 percent of the time patients are saying they are satisfied after five years.

DR. WHALEN: I would like to thank the sponsor then and ask that Ms. Allen and Dr. Dawisha again come forward for the FDA presentation.

FDA Presentation

MS. ALLEN: Good afternoon. FDA will now summarize the status of the conditions of approval for Inamed saline-filled breast implant PMA. For your convenience, we have provided you with a hard

copy of FDA slides.

There are five conditions of approval, a post-approval study, a focus group study, a retrieval study, fatigue testing and shelf-life testing.

Dr. Sahar Dawisha will present the status of the post-approval study and I will present the status of the remaining four conditions of approval. I will now hand it over to Dr. Dawisha.

DR. DAWISHA: Good afternoon. Recall that the A95 and R95 studies, which the PMA was based on, were five-year studies with three-year data presented to the panel back in March of 2000.

The sponsor has now followed this patient cohort for the total of the five years of the study, and they are going to be following the patients in an abbreviated protocol for the remainder of the five years, for ten years. The database was closed for this update in August of 2001, and I am going to be discussing augmentation, followed by reconstruction.

Table 1 shows the patient follow-up at five years for augmentation on an by-patient basis. The percent follow-up of 81.1 percent, which is defined as the actual follow-up of 686 patients

divided by the expected follow-up of 846 patients, is shown here, as well as the reasons for withdrawals.

This slide summarizes the by-patient cumulative Kaplan-Meier risk rates for selected complications with corresponding 95 confidence intervals. The three-year data in this table is what is currently reported in the approved labeling, and the five-year data is the updated information which is going to be included in the updated labeling.

Compared to three years, the rates at five years are slightly higher, however, the confidence intervals are overlapping. The exception to this is for the complication of implant removal where the confidence intervals are not overlapping, suggesting a significantly increased cumulative rate at five years compared to three. I will be discussing implant removal in more detail later in the presentation. Just to note that infection is not included here. The five-year Kaplan-Meier rate for infection was one percent.

The number and types of additional surgical procedures performed in the augmentation patients is shown through four years, which is what

is currently reported in the labeling, and through five years as an update.

Through five years, there were a total of 463 additional surgical procedures performed at 293 reoperations in 224 of the 901 augmentation patients enrolled in the study. Of the 224 patients undergoing reoperation, the majority, 82 percent, underwent one reoperation. Through both four and five years, implant removal for any reason with replacement was the most commonly performed additional surgical procedure, constituting approximately one-third of the procedures. It was 30.3 percent through four years and 33.7 percent at five years.

This is followed by capsule procedures, specifically capsulotomy, which constituted the majority of the capsule procedures. There was about three-quarters of the capsule procedures at both four and five years.

Of the 1800 augmentation implants that were enrolled in the A95 study, there were 166 implant removals, or 9.2 percent, through five years for any reason. On a by-patient basis, there were 10.9 percent of patients who had an implant removed through five years for any reason.

The primary reason for implant removal, using the same hierarchy as in the currently approved labeling, is shown on this slide. I have combined categories for the purpose of projecting the slide, as noted in the footnotes below the table. Patient request constitutes approximately less than half of the primary reasons for implant removal through both four and five years. It is 43.2 percent at four years and 42.2 percent at five years. The majority of these patient requests for an implant size or shape change.

Of the complications, leakage or deflation constitutes the most frequent primary reason, approximately 33 percent at both four and five years.

For those patients who underwent implant removal with replacement, i.e., who had a revision and had follow-up, selected complications follow-up implant replacement are shown on this table at two years, which is what is currently reported in the labeling and at three years which is the updated information. Although the Kaplan-Meier rates are higher at three years than at two years, the confidence intervals are overlapping, suggesting that the rates are not significantly different.

I would like to point out that for implant removal and/or replacement the overlap is minimal, suggesting that the rate at three years is approaching the limit of being significantly higher than at two years.

The sponsor provided updated information pertaining to breast disease and connective tissue disease, however, I am not going to be discussing these results.

We now move on to the reconstruction data. The patient follow-up for the reconstruction patients is shown on this table through five years. Again, the percent follow-up, which is the actual follow-up divided by the expected is 80 percent.

The next table shows the by-patient cumulative Kaplan-Meier rates of first occurrence through three years, which is what is currently reported in the labeling, and through five years, which is the updated information for selected complications. Although the rates at five years are slightly higher than at three years, the confidence intervals for all these complications are overlapping, suggesting no significant differences. Note that the reoperation rate here excludes planned procedures as part of stage

reconstruction.

Table 8 summarizes the number and types of additional surgical procedures excluding planned procedures through four years, which is what is reported in the current labeling, and through five years, which is the updated information. There were a total of 159 additional surgical procedures performed and 126 reoperations in 100 of the 237 percents enrolled in the R95 study. Of the 100 patients undergoing reoperation, the majority, 81 percent, underwent one reoperation. Through both four and five years, implant removal for any reason, with replacement, was the most commonly performed additional surgical procedure, constituting approximately 30 percent of the procedures through five years. This is followed by skin or scar revision or removal, 27.7 percent, and followed by implant removal without replacement, 13.2 percent.

Of the 316 implants in the R95 study, there were 70 implants which were removed, which is 22.2 percent, through five years for any reason. On a by-patient basis, there were 26 percent of patients who underwent implant removal through five years for any reason. The primary reason for

implant removal in this group, using the same hierarchy as in the currently approved labeling, is shown here, and through both four and five years capsular contracture constitutes the largest primary reason for implant removal, approximately 26 percent at four years and 31 percent at five years. This is followed by patient request for a size or shape change, approximately 23 percent at four years and 21 percent at five years. Then, followed by leakage/deflation, 16 percent through four years and 17 percent through five years.

For those patients who underwent implant removal with replacement, i.e., who had a revision and then had follow-up, selected complications are shown here. Although the Kaplan-Meier rates at three years are higher than at two years, the confidence intervals are again overlapping, suggesting that the rates are not significantly different.

This concludes my presentation and now Ms. Allen will continue with the focus group study results.

MS. ALLEN: The ultimate goal of the focus group study was to improve their existing patient brochure. Inamed already described how an

independent study was conducted to obtain feedback regarding their patient brochure. They also described some of the key findings from that independent study.

FDA considered the independent study reports submitted by both Mentor and Inamed and required the same types of changes for both companies, if applicable. The primary changes to Inamed's patient brochure were as follows: They made significant modifications to the lead-ins, as well as to the content of the safety tables because the majority of the women found the information confusing. They stratified the augmentation and reconstruction information. They added a table of contents and a glossary, and they modified the graphics to read easier.

Inamed incorporated all requested changes into the patient brochure and received FDA approval. Therefore, we consider this condition of approval fulfilled. Inamed has just submitted a revised patient brochure and package insert that reflect the five-year post-approval data. After FDA review and approval, Inamed with finalize them for patient and product use.

The purpose of the retrieval study is to

determine modes of failure. This information may lead to changes in manufacturing design specifications, mechanical testing requirements, and/or labeling.

In their 2001 report, Inamed submitted data on over 2400 explants collected over an eight-month period. They provided clinical or physician observations collected at the time of explantation. They provided laboratory observations or device failure characteristics, such as smooth and sharp crease-edge openings. These were noted with respect to whether the device was deflated or non-deflated. They also provided material property test data.

Inamed made numerous conclusions regarding whether the device failure characteristics were representative of a true failure or the result of an artifact. These were summarized by Inamed earlier and provided in your panel memo.

Inamed made on hypothesis regarding a mode of failure. That is, based on smooth-edge openings being a characteristic found more in smooth shells, failure may be caused by fold flaw and repetitive abrasion of both sides of the shell.

Inamed will submit a final report of the

retrieval study in their 2002 annual report. Therefore, FDA considers this condition of approval still open.

The purpose of the fatigue testing was to determine the fatigue strength of Inamed's product line. These data provide additional information on the expected long-term performance of the device.

Of the five styles in their product line, Inamed performed fatigue testing on styles 68 and 168 as representative of their entire product line. The resulting endurance load limit was 20 lbs at 6.5 million cycles run-out for both styles, which met the acceptance criteria.

As part of the test report, Inamed also supplied the ultimate static rupture results for those two styles. The results were over 1600 lbs for both styles, which shows that the implants failed at static loads much greater than that expected during mammography, which is 55 lbs. FDA considers this condition of approval fulfilled.

The purpose of the shelf-life testing is to support a five-year expiration date on the package label. Inamed's shelf-life protocol involves real-time package integrity and mechanical testing performed at year zero, or baseline, and

annually through five years.

In their 2001 annual report, Inamed provided an interim report with year zero data. The results were adequate. FDA expects Inamed to submit an updated report of shelf-life testing annually until the desired five-year expiration date is supported. Therefore, FDA considers this condition of approval still open.

This is an overall summary of Inamed's five conditions of approval. The post-approval study will remain open until five-year data are submitted. The focus group study is complete. Inamed has already revised their patient labeling to reflect the focus group study findings. The retrieval study is currently open, however, Inamed will submit the final report in July, 2002. The fatigue testing is complete. The shelf-life testing will remain open until five-year data are submitted.

I will now turn it over to the panel for discussion.

DR. WHALEN: Thank you both Ms. Allen and Dr. Dawisha. Let me add, Dr. Dawisha, if I had had someone with your gift of lucidly turning numbers into knowledge in med school, I might not have

developed a life-long passionate hatred of biostatistics. So, thank you very much.

[Laughter]

Are there any questions of the FDA members? Yes, Dr. DeMets?

DR. DEMETS: Although the sponsor didn't say this directly, you certainly allude to the fact that because the confidence intervals overlap there was no significant difference, which is technically true but the other side of the story is was the study big enough to have sensitivity to find differences of that size? So, I am not quarreling with the general gist or your comment, but I think the only caution in pushing that statement too far is, yes, they may not be statistically different but it could be that the difference is there and you just can't see it with the size of the study, or maybe there isn't a difference. That is just a caution, and I think somewhere in all the discussion we need to have some discussion or comment on the size of the study, the precision that they are able to find for the different outcomes, whether it is failure rate or other kinds of complications.

DR. DEMETS: Yes, I would agree. We

actually did not ask the sponsor to do statistics for that reason. That is why I didn't present statistics but we were just sort of trying to make some sort of comparison of time trend analysis.

Panel Discussion

DR. WHALEN: Other questions?

[No response]

Thank you very much. We would like now to have discussion by each of the panel members, the last go around the table for this particular presentation. I think it is only fitting that at our last meeting Dr. Chang has the last words so we will start with Dr. Miller and then work our way around the table. Dr. Miller?

DR. MILLER: I guess I would like, first of all, to compliment this afternoon's presentations. I certainly feel much more satisfied with the data presented this afternoon, and reassured by it.

I think I would like to emphasize as we consider these things that this is a unique set of patients and unique problem, and looking at single things like reoperation, which ordinarily we would consider something undesirable for most surgical procedures, for most procedures like this,

reconstruction procedures or esthetic procedures, it is almost expected that there will be other procedures performed to achieve the desired result. So, looking at that as an isolated category and considering it a complication per se is not really interpreting it properly. So, I just would like to be cautious about that.

The other thing I would like to point out is that the satisfaction levels being high, despite a 40 percent incidence of reoperations, just points out this sort of elusive side of this problem, the benefit perceived by the patient. Ordinarily, a reoperation would lower a person's satisfaction with what they are going through perhaps, and it does at the time, but patients perceive a tremendous benefit from having these procedures, even with multiple procedures. So, we have to remember that as we consider the risk/benefit ratio on the use of the implants. But this kind of data is very helpful to get an idea about what the risks side of the equation is.

DR. WHALEN: I should just state if you two are more comfortable not being in the center, since you have already completed, feel free to adjourn, but we are delighted to have you where you

are as well. Ms. Brown?

MS. BROWN: This is my first panel meeting at which the breast implants have been discussed, so I don't have the benefit of the history of being at the last meetings. One of the things I am very pleased to see was a requirement and was actually fulfilled is the evaluation of the patient brochures, the focus groups, because adequately informing the patients of the risks as well as the benefits of the procedure seems to be a key to ensuring future satisfaction of patients. I guess I would take that as an indication that that is probably a reasonably successful process of the patient brochure informing the patients because the satisfaction rates have been pretty high in spite of the complication rate.

So, I would just exhort the companies to continue to keep an eye on that patient brochure process, keeping that information up to date.

DR. WHALEN: Dr. Doyle?

DR. DOYLE: I would like to thank the presenters this afternoon for a very clear presentation. My only concern is that they have gotten such an excellent follow-up rate with the procedure they have been using to date, which is

the physician visit, and they are now going to switch to another procedure. I would wish, if it were at all possible, that they try to continue to go through the physician because the follow-up rate, I fear from other studies, will fall off drastically for the next five years, and it is so important to have those data in the longer-term follow-up. If it were at all possible, I would hope that they would be able to continue to go through the physician because I think that this kind of data set--this is an amazingly good follow-up for this particular type of group of women.

I think it is interesting, as Dr. Miller noted, that the patients are satisfied even though there is a high complication rate, I think similar to some of the injectable contraceptives where there was 80-90 percent breakthrough bleeding and, yet, the satisfaction was very high. So, it speaks again to the fact that is an individual's decision and, as long as they have the right information on which to make that decision, I feel that they have the right to make it and I would continue to urge that we give them the correct data.

DR. WHALEN: Dr. McCauley?

DR. MCCAULEY: I would like to basically echo some of the comments that have already been made. I think Inamed is to be congratulated on their presentations and their clarity, and also the follow-up that they have been able to sustain at five years on their patients.

I would only suggest that at least with the focus group study, after revisions are made in those brochures, to actually take those back to those patients for follow-up just to make sure that the changes that they perceived to be resolved or clarified the brochure a little bit better are actually the same as what the patients actually think. I think that is an important but I think overall it was an excellent presentation. I think their data actually resolve some of the issues that were of tremendous concern prior to their presentation.

DR. WHALEN: Dr. Dubler? I am the only survivor of the '92 hearings and the hearings two years ago and today, and it is heartening. I thought the PMA data that were presented two years ago were excellent and today's follow-up has been equally excellent, and I thank you for that.

For the FDA, I would suggest, and I don't

know how we would do this, but these data and the patient brochure are the basis for an informed consent process but they are not the informed consent process. That has to go on with the physicians, and I don't know if there is any way of trying to affect, change or help that process to evolve into one that uses these data and truly empowers patients. Maybe that is beyond what the FDA can consider, but there is such a nice platform now to help women think about this decision that it would be excellent if we could take that to the next step, if the FDA could encourage that process of informed consent to go forward. So, I thank you for the data. They are very helpful, and for a clear presentation.

DR. WHALEN: Dr. Choti?

DR. CHOTI: Although many of the points have been clarified this afternoon, I still think it is important to emphasize what we have been talking about all day, and that is, this is a common operation being performed with placement of this device with increased frequency, often in healthy women, and there is still a significant paucity in data to help both the physician and the patient make informed decisions.

Although this data certainly was presented quite clearly, I think I would still encourage the increase in quality, follow-up data, preferably independently collected, longer-term follow-up. Also, I agree with using that information as well as continued focus groups to continue to improve informed consent because it is still not clear whether this information is really being understood by the woman who is getting these implants put in.

DR. WHALEN: Dr. Newburger?

DR. NEWBURGER: I appreciate the seriousness with which Inamed has taken the FDA's directives, and the thoroughness with which the follow-up studies have been applied. I hope that Inamed will apply the same thoroughness to improving product performance to have less leakage developing, less reactivity of the implants because still, when you look at the rate of leakage of 10, 11 percent over five years, this still translates, at the current rate of implantation, into between 20,000 and 30,000 women having this complication and them having to have a reoperation. So, I hope you will apply the same thoroughness and diligence in further perfecting the product. But thank you very much.

DR. WHALEN: Dr. DeMets?

DR. DEMETS: Well, I would like to echo the sentiments of my previous colleagues speaking. I was very pleased, for example, that the follow-up was based on clinic evaluations. I share Dr. Doyle's concern that if you switch procedures it may drop. Obviously, there are some practical matters that have to be taken into consideration.

I have already said my comment about response rates. I think this is a substantial improvement in the right direction. I think because of the sensitivity and the interest of this particular study and this device, my own personal view is that an 80 percent response rate is probably not good enough to get rid of some of the concerns because with 20 percent non-response there is plenty of room for bias, and I can't predict which way the bias will go. It could go in favor of or against the device because it is very hard to predict those kind of things. But 20 percent is a lot of room. If you have 80 percent now at five years, I worry about what it will be at ten years even if you didn't change procedures, and I worry even more if you do.

So, I guess my recommendation or at least

suggestion to the sponsor is to work even harder to get those rates up. I think it will serve you well in the long-run to address controversies and questions that are bound to come.

I guess this is my last meeting so I am allowed to not follow the rules totally, but if I were in the business of breast implants in any way, I think I would demand that some kind of registry--if there are 300,000 of these per year, it would be of benefit of the investigators, patients, sponsors and even the FDA to have some national registry of these kind of patients so we really get the kind of numbers and the kind of follow-up and the conditions that if you get into the registry you have to stay in the registry so we good, complete--otherwise, this controversy will be here five years from now just as sure as it is right now.

That would be a general plea to everybody. It is an important area, obviously, and everybody cares about this, so that would be my general plea.

Finally, and a personal comment, I just want to thank the panel for allowing a biostatistician to survive four years amongst a group of surgeons, and occasionally pay attention

to what I say or at least the points I am trying to make. So, I thank the panel for tolerating me for four years, and for the FDA allowing me to be a member of this committee.

DR. WHALEN: Dr. Chang?

DR. CHANG: In March of 2000 I felt that McGhan Medical Corp. had done its homework in presenting data for its PMA evaluation. I believe that Inamed has shown due diligence in the follow-up and presenting the data as part of its approval conditions. So, I want to commend the sponsor for the data that they have presented today.

A continued plea, and I would echo what Dr. Newburger says, is let's not rest on our laurels. I make an appeal to sponsor to continue to use its energies and resources to improve on the rate of leakage and deflation. And, whether this includes physician education, a warning not to under-inflate to try to prevent the folding that can occur because of position usage, that may be an important part of decreasing the rate. Regardless of this, again, there is room for improvement but I do want to congratulate the sponsor for doing an excellent presentation today, and I would like to

thank FDA again for the opportunity to participate these past few years on the panel.

DR. WHALEN: Thank you. Dr. Witten, is the discussion satisfactory to FDA?

DR. WITTEN: Yes, it is.

DR. WHALEN: Thank you. Let me add a thanks to all of those who testified, particularly this morning during the public session. I realize many of them took their own time and some of them their own financial resources to bring a very impassioned and heartfelt message to us, and I assure you we did hear what you had to say to us and have taken that into consideration.

I would like to thank all of my fellow panel members, from very solid new additions to the panel to always stalwart temporary panel members, and give special thanks to Drs. Chang and DeMets for their service elbow to elbow with me for the past few years.

Finally, let me give my profound thanks to the FDA. Between 12 years active and 16 years reserve service in the United States Navy, I have somehow developed a moderately cynical attitude towards the government--hard to believe. Despite that, the FDA has consistently, at every

level--scientific review, leadership, professional, administrative and support--always done an impeccable job, and they have done it in a fishbowl. It has to be this way; it should be this way, but every watchdog group and every congressional member of the Hill is watching you guys every time you use a pencil eraser. So, my hat is off to you.

Having completed our business, this meeting of the General and Plastic Surgery Devices Panel is adjourned.

[Whereupon, at 2:55 p.m., the panel was adjourned]

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CERTIFICATE

I, **SONIA GONZALEZ**, the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.

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